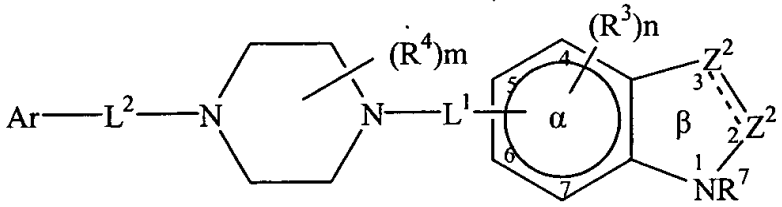
CLAIMS AMENDMENT

1. (currently amended): A compound of the formula:



(1)

and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

represents a single or double bond;

one Z^2 is CA or CR^8A and the other is CR^1, CR^1_2, NR^6 or N wherein each R^1, R^6 and R^8 is independently hydrogen or noninterfering substituent;

A is $-W_i-COX_jY$ wherein Y is COR^2 ~~or an isostere thereof and~~ wherein R^2 is hydrogen or ~~a noninterfering substituent~~ is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, CN, COOR, $CONR_2$, COR, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the forms thereof containing 1-2 O, S and/or N atoms, or

wherein R^2 is OR, NR_2, $NRCONR_2$, $OCONR_2$, $NRSO_2NR_2$, heteroarylalkyl, COOR, $NRNR_2$, heteroaryl, heteroaryloxy, heteroaryl-NR_2, or NROR wherein each R is independently H, alkyl, alkenyl or aryl or the forms thereof containing 1-2 O, S and/or N atoms, and wherein two R attached to the same atom may form a 3-8 member ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR_2, OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCONR_2$, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the forms thereof containing 1-2 O, S and/or N atoms wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined, and

each of W and X ~~is a spacer of 2-6Å which~~ is substituted or unsubstituted alkylene, alkenylene or alkynylene, each of 2-6Å or

Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole and each of i and j is independently 0 or 1;

R^7 is H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, or heteroalkyl, ~~heteroalkenyl, heteroalkynyl, heteroalkylaryl,~~ said heteroalkyl containing 1 or 2 O, N and/or S, or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$, SO_2NR_2, CN, CF_3, NR_2, OR, alkyl-SR, alkyl-SOR, alkyl-SO_2R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-$CONR_2$, or R_3Si, wherein each R is independently H, alkyl, alkenyl or aryl or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms;

each R^3 is independently a noninterfering substituent;

n is 0-3;

~~each of~~ L^1 is CO, SO_2 or alkylene (1-4C); ~~[[and]]~~

L^2 is ~~independently~~ alkylene (1-4C) or ~~alkenylene (1-4C)~~ alkenylene (2-4C) optionally substituted with ~~a moiety~~ one or two moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, ~~heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl,~~ NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, ~~alkyl-OOR~~ alkyl-OOCR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, and R_3Si, ~~and NO_2,~~ wherein each R is independently H, alkyl, alkenyl or aryl or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms, and wherein two substituents ~~on L^1 or~~ on L^2 can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety;

each R^4 is independently a noninterfering substituent;

m is 0-4;

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two adjacent noninterfering substituents can form a fused ring of 3-8 members; ~~and~~

~~the distance between the atom of Ar linked to L^2 and the center of the α ring is 4.5-24Å.~~

2-4. (canceled)

5. (original): The compound of claim 1 wherein each of i and j is 0.

6. (original): The compound of claim 2 wherein j is 0.

7-8. (canceled)

9. (currently amended): The compound of claim 1 wherein R^7 is H, or is optionally substituted alkyl[[,]] or acyl.

10-11. (canceled)

12. (currently amended): The compound of ~~claim 11~~ claim 1 wherein L^1 is CO.

13-15. (canceled)

16. (previously presented): The compound of claim 1 wherein L^2 is unsubstituted alkylene and L^1 is CO.

17. (previously presented): The compound of claim 1 wherein L^2 is unsubstituted methylene, methylene substituted with alkyl, or -CH= and L^1 is alkylene or CO.

18. (currently amended): The compound of claim 1 wherein Ar is optionally substituted with 0-5 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, ~~heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl,~~ NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

19. (original): The compound of claim 18 wherein Ar is optionally substituted phenyl.

20. (original): The compound of claim 19 wherein said optional substitution is by halo, OR, or alkyl.

21. (original): The compound of claim 20 wherein said phenyl is unsubstituted or has a single substituent.

22. (currently amended): The compound of claim 1 wherein R^4 is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, ~~heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl,~~ NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms and two of R^4 on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R^4 is =O or an oxime, oximeether, oximeester or ketal thereof.

23. (original): The compound of claim 22 wherein each R^4 is halo, OR, or alkyl.

24. (original): The compound of claim 23 wherein m is 0, 1, or 2.

25. (original): The compound of claim 24 wherein m is 2 and both R^4 are alkyl.

26. (currently amended): The compound of claim 1 wherein each R^3 is halo, alkyl, ~~heteroalkyl,~~ OCOR, OR, NRCOR, SR, or NR_2, wherein R is H, alkyl, aryl, or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms.

27. (original): The compound of claim 26 wherein R^3 is halo or alkoxy.

28. (original): The compound of claim 27 wherein n is 0, 1 or 2.

29. (original): The compound of claim 1 wherein L^1 is coupled to the α ring at the 4-, 5- or 6-position.

30. (previously presented): The compound of claim 1 wherein Z^2 at position 3 is CA or CHA.

31. (original): The compound of claim 30 wherein the Z^2 at position 2 is CR^1 or CR^1_2.

32. (currently amended): The compound of claim 31 wherein R^1 is hydrogen, or is alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, ~~heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl,~~ NH-aroyl, halo, OR, NR_2, SR, SOR, SO_2R, OCOR, NRCOR, $NRCONR_2$, NRCOOR, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R, $CONR_2$, SO_2NR_2, $NRSO_2NR_2$, CN, CF_3, R_3Si, and NO_2, wherein each R is independently H, alkyl, alkenyl or aryl or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms ~~and two of R^1 can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members~~.

33. (currently amended): The compound of claim 32 wherein each R^1 is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, ~~heteroalkyl,~~ heteroaryl, halo, OR, NR_2, SR, NRCOR, alkyl-OOR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms.

34. (original): The compound of claim 30 wherein Z^2 at position 2 is N or NR^6.

35. (currently amended): The compound of claim 34 wherein R^6 is H, or alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, or heteroaryl, ~~heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl,~~ or is SOR, SO_2R, RCO, COOR, alkyl-COR, SO_3R, $CONR_2$, SO_2NR_2, CN, CF_3, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or ~~heteroforms~~ forms thereof containing 1-2 O, S and/or N atoms.

36. (original): The compound of claim 1 wherein  represents a double bond.

37-38. (canceled)

39. (currently amended): A pharmaceutical composition for treating pathological conditions characterized by ~~enhanced~~ excessive p38-α activity which composition comprises a therapeutically effective amount of a compound claim 1 or the pharmaceutically acceptable salts thereof, along with a pharmaceutically acceptable excipient.

40-41. (canceled)

42. (previously presented): A method to treat rheumatoid arthritis comprising administering to a subject in need of such treatment a compound of claim 1 or the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof.

43-44. (canceled)

45. (previously presented): The compound of claim 36, wherein Z^2 at position 3 is CA.

46. (previously presented): The compound of claim 45, wherein Z^2 at position 2 is CR^1.

47. (currently amended): The compound of claim 46, wherein A is $COCOR^2$, wherein R^2 is as defined in claim 1.

48. (canceled)

49. (currently amended): The compound of ~~claim 48~~ claim 47, wherein R^1 is H.

50. (previously presented): The compound of claim 49, wherein n is 0 or 1.

51. (previously presented): The compound of claim 50, wherein Ar is substituted phenyl.

52. (currently amended): The compound of claim 51, wherein L^2 is unsubstituted or substituted alkylene ~~optionally including a heteroatom~~.

53. (previously presented): The compound of claim 52, wherein L^1 is alkylene or CO.

54. (previously presented): The compound of claim 53, wherein L^2 is methylene and L^1 is CO.

55. (previously presented): The compound of claim 54, wherein n is 1 and R^3 is halo or methoxy.

56. (previously presented): The compound of claim 55, wherein R^7 is H or alkyl.

57. (previously presented): The compound of claim 56, wherein R^7 is methyl.

58. (previously presented): The compound of claim 57, wherein Ar is para-fluorophenyl.

59. (currently amended): The compound of claim 58, wherein R^2 is OR, NR_2, SR, $NRCONR_2$, $OCONR_2$ or $NRSO_2NR_2$ wherein each R is independently H, alkyl, alkenyl or aryl or the ~~heteroatom containing~~ forms thereof containing 1-2 O, S and/or N atoms and wherein two R attached to the same atom may form a 3-8 membered ring.

60. (currently amended): The compound of claim 59, wherein R^2 is NR_2 wherein each R is independently H, alkyl, alkenyl or aryl or the ~~heteroatom containing~~ forms thereof containing 1-2 O, S and/or N atoms and wherein two R attached to the same atom may form a 3-8 membered ring.

61. (previously presented): The compound of claim 60, which is selected from the group consisting of compound Nos. 15, 33, 57, 59, 77, 89, 96, and 100 of Table 2, *i.e.*,

1-methyl-6-methoxy-[4′-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalicamide;

1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N-methyl-glyoxalicamide;

1-methyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide; and

1-methyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

62. (previously presented): The compound of claim 60, wherein said compound is compound No. 15 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4′-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

63. (previously presented): The compound of claim 60, wherein said compound is compound No. 33 of Table 2, *i.e.*, 1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

64. (previously presented): The compound of claim 60, wherein said compound is compound No. 57 of Table 2, *i.e.*, 1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

65. (previously presented): The compound of claim 60, wherein said compound is compound No. 59 of Table 2, *i.e.*, 1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalicamide.

66. (previously presented): The compound of claim 60, wherein said compound is compound No. 77 of Table 2, *i.e.*, 1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N-methyl-glyoxalicamide.

67. (previously presented): The compound of claim 60, wherein said compound is compound No. 89 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

68. (previously presented): The compound of claim 60, wherein said compound is compound No. 96 of Table 2, *i.e.*, 1-methyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

69. (previously presented): The compound of claim 1, wherein said compound is compound No. 162 of Table 2, *i.e.*, 6-chloro-[4′-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

70. (previously presented): The compound of claim 60, wherein said compound is compound No. 100 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

71. (previously presented): The compound of claim 1, wherein said compound is compound No. 17 of Table 2, *i.e.*, 1-ethoxycarbonyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

72. (previously presented): The compound of claim 1, wherein said compound is compound No. 38 of Table 2, *i.e.*, 1-ethoxycarbonyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

73. (previously presented): The compound of claim 1, wherein said compound is compound No. 45 of Table 2, *i.e.*, 1-t-butoxycarbonyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

74. (previously presented): The compound of claim 1, wherein said compound is compound No. 56 of Table 2, *i.e.*, 1-acetyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

75. (previously presented): The compound of claim 1, wherein said compound is compound No. 60 of Table 2, *i.e.*, 1-acetyl-2-methyl-6-methoxy-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

76. (previously presented): The compound of claim 1, wherein said compound is compound No. 63 of Table 2, *i.e.*, 1-methoxymethyl-6-chloro-[4′-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

77. (previously presented): The compound of claim 1, wherein said compound is compound No. 92 of Table 2, *i.e.*, 1-methoxymethyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

78. (previously presented): The compound of claim 1, wherein said compound is compound No. 102 of Table 2, *i.e.*, 1-methyl-6-chloro-[4-(1-4'-fluorophenylethyl)piperazinyl]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

79. (previously presented): The compound of claim 1, wherein said compound is compound No. 137 of Table 3, *i.e.*, 6-methoxy-(4-benzyl piperazinyl)-indole-5-carboxamide-3-glyoxalic acid-methyl ester.

80. (previously presented): The compound of claim 1, wherein said compound is compound No. 138 of Table 3, *i.e.*, [4-(1-phenylethyl)piperazinyl]-indole-5-carboxamide-3-glyoxalic acid methyl ester.

81. (previously presented): The compound of claim 1, wherein said compound is compound No. 152 of Table 3, *i.e.*, (4-benzyl-2R,5S-piperazinyl)-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

82. (previously presented): The compound of claim 1, wherein said compound is compound No. 161 of Table 3, *i.e.*, 6-methoxy-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

83. (previously presented): The compound of claim 1, wherein said compound is compound No. 177 of Table 3, *i.e.*, 6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

84. (previously presented): The compound of claim 1, wherein said compound is compound No. 180 of Table 3, *i.e.*, (6-methoxy[4-(1-4'-fluorophenylethyl)piperazinyl)-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

REMARKS

The specification has been amended to delete an unnecessary and apparently confusing definition of "alkylene."

The claims have been amended substantially as agreed at the interview to expedite prosecution. The definition of R^2 as set forth in claim 2 has been inserted into claim 1; those embodiments set forth on page 10, lines 20-22, have been included as well. The formula for $NRNR_2$ has been corrected. As requested, the term "heteroalkyl" has been deleted from the definition. The definition of R in the substituents as H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof has been retained but clarified based on the definition set forth on page 6, at lines 3-4, which indicates alkyl, alkenyl, etc. may be in a form that contains 1-2 O, S or N heteroatoms or combinations thereof. This possibility must be included to accommodate, for example, compounds 28-32 and 34-36 where R^2 is NR_2 and two R attached to the nitrogen form a 3-8 membered ring. One of the R groups must contain an heteroatom in order to form the morpholine or piperazine ring shown in these compounds.

This modification has been done consistently throughout the claims.

The definition of W and X has been reworded, as agreed at the interview, to delete reference to a "spacer." It is understood that, under these circumstances designating the length of the alkylene, alkenylene or alkynylene as 2-6Å is acceptable.

The alternative definition of Y from claim 4 has also been inserted into claim 1.

Moving down the set of definitions, L^1 has been redefined as CO, SO_2 or alkylene. This definition is consistent with that in currently pending claims 17 and 53, not objected to by the Office; SO_2 is included as an isostere of CO (see page 7, line 12 of the specification). It is also consistent with the description on page 6, lines 30-31, which states that L^1 and L^2 are CO or

isosteres thereof or optionally substituted isosteres or longer chain forms. It is believed understood that although L^2 "in particular" may be alkylene or alkenylene, this is understood to apply to L^1 as well since otherwise the remainder of the sentence "or L^1 or L^2 may be or may include a heteroatom such as N, S or O." on page 7, lines 1-2, would not make sense.

Also in claim 1, the definition of L^2 has been amended to delete "heteroalkyl, heteroalkenyl, heteroalkynyl and heteroalkylaryl" to accommodate the Examiner's request made at the interview. Although there is no outstanding written rejection to these terms; this amendment is made in order to expedite prosecution. "Heteroalkyl" has not been deleted from the definition of R^7 in claim 1, however, in light of the large number of compounds that illustrate this embodiment and in light of the definition of heteroalkyl on page 6, lines 2-4. For example, compounds 43, 51, 62-63, 92, 99, 70, 76, 91, 93 and 94 are all heteroalkyl substituents representing R^7. "One or two" has been substituted for "a" in describing the number of substituents permitted on L^2 consistent with page 7, line 13 of the specification.

The limitations set forth on page 7 with regard to adjacent substituents forming a fused ring on Ar have also been added and the limitation on the distance between the atom of Ar linked to L^2 in the center of the α ring has been deleted from the claims as now unnecessary.

Other claims which contain "heteroalkyl," etc. designations have been amended to respond to the objection raised at the interview; these include claims 18, 22, 32, 33, 35 and 52. Claim 32 has also been amended to remove an unnecessary embodiment.

As further agreed at the interview, claim 37 has been canceled and claims 40-41, which were withdrawn from consideration, have been canceled as well.

Claim 48 has been canceled as redundant with the definition of R^2 now in claim 1.

No new matter has been added and entry of the amendment is respectfully requested.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 1 was rejected under this section on a number of grounds which, it is believed, are addressed adequately by amendment and the following remarks. First, the term "isostere thereof" with respect to COR^2 no longer appears in claim 1; instead, the specific isosteres set forth in claim 4, which was not objected to, have been inserted. Second, "non-interfering substituents" is objected to, but no explanation is given. The nature of "non-interfering substituents" has been set forth on page 5 in detail. It is believed that this term is clear in the context of the present claims, and unless there is some basis for making this rejection, applicants believe the term should remain in the claims. Applicants appreciate that it was evidently agreed at the interview that this term could remain in the claim with the exception that the substituent R^2 was required to be defined. Further specificity with regard to the definition of R^2 now appears in the claim.

"Each of W and X is a spacer of 2-6 Å" has been replaced by rewording that was agreed upon at the interview. W and X are now defined as substituted or unsubstituted alkylene, alkenylene or alkynylene and the distance specification simply limits the number of carbons in the chain.

"Ar is an aryl group substituted with 0-5 non-interfering substituents wherein two non-interfering substituents can form a fused ring" has been replaced by clarifying language. Although no explanation is given for this objection in regard to the rejection under § 112, paragraph 2, it appears that the basis is that the description on page 7 of the specification, lines 29-31, is required, as set forth under the rejection made under 35 U.S.C. § 112, first paragraph. In any event, these limitations have been provided.

Finally, "the distance between the atom of Ar linked to L^2 in the center of the α ring is 4.5-24 Å" is objected to. This limitation no longer appears in the claims as it appears

unnecessary in light of the definitions of L^1 and L^2. It is believed that the amendment and discussion dispose of the rejections made under this statutory section.

The Rejection Under 35 U.S.C. § 112, First Paragraph

Only claim 1 was criticized or rejected under this statutory section. The first rejection relates to alleged new matter concerning substituents on adjacent positions of Ar to form a fused ring of 3-8 members. The claim has been amended to conform to the limitations in the specification. Thus, it is believed that this basis for rejection is moot.

The second basis for rejection has to do with the infamous definition of alkylene, as $-(CH_2)_n-$ on page 3. This definition has been removed by amendment. Such removal is not new matter. The Office has continued to insist that the n *in this context* must be 0-3 because n in an *entirely different context* (as the number of R^3 substituents in the formula of claim 1) is defined that way. Respectfully, it is not believed readers would interpret these two designations of n to refer to the same thing. It would be recognized that the "n" in the formula $-(CH_2)_n-$ is a generic designation meaning an undetermined number and totally undefined. In view of the amendment to delete this phrase and in view of the agreement reached at the interview, it is believed that this issue has been resolved.

Applicants have already explained the origin of the limitation (1-4C) in previous responses but to repeat, alkyl is repeatedly defined as (1-4C) for example, on page 9, line 4, page 9, line 23 and page 10, line 25. In defining W and X, on page 10, the word "alkyl" is again used, although it is clear from the position of W and X in the molecule that the "alkyl" group must be divalent. However, because the same word was used, it should be clear that it is the intent to define the divalent form in the same manner. Accordingly, (1-4C) as applied to the divalent form of alkyl is not new matter.

As to alkenylene, of course, there must be a minimum of two carbons in order to accommodate the π bond. Again, in view of the agreement reached at the interview, this issue appears resolved as well.

The remainder of this rejection asserts that two substituents only on L^2 (not L^1) have been disclosed as able to form a non-aromatic saturated or unsaturated ring, etc. Claim 1 has been amended accordingly and thus this basis for rejection is moot.

Finally, the Office objects to the distance designation of 4.5-24 Å; there is no basis given in this explanation with regard to 35 U.S.C. § 112, First Paragraph, rather the rationale appears to be reflective of a Second Paragraph rejection. Nevertheless, this objection is moot in view of the amendment to the claims.

Based on the foregoing discussion and the amendment to claim 1, it is respectfully submitted that the rejection of this claim under 35 U.S.C. § 112, First Paragraph, may properly be withdrawn.

Claims Not Rejected Over the Art

None of claims 2-6, 9, 11-12, 16-37, 39 or 45-84 were rejected over the art. Accordingly, applicants believe that these claims are clearly in a position for allowance once the double-patenting rejections set forth below are addressed.

The Art Rejection

Only claim 1 was rejected over the art. As the limitations of claims 2 and 53, neither of which was rejected over the art, have been inserted into claim 1, it is believed the art rejection is moot. However, for completeness, applicants will discuss this basis for rejection, briefly.

Claim 1 was rejected as assertedly unpatentable over Japanese application JP 61-291566 in view of CRC Handbook. Applicants respectfully point out that there are quite a few

differences structurally between the compound focused on by the Office in the Japanese application and the compounds of claim 1:

1) The compounds of the Japanese application (at least as set forth on the English abstract kindly supplied by the Examiner) are benzofurans and the compounds claimed here are benzimidazoles.

2) The compounds of the present invention comprise a piperazine ring between the benzimidazole and the aryl moiety. The Japanese application compound (at least as shown in the abstract) does not have any piperazine nucleus or any counterpart of it.

3) The compounds disclosed in the Japanese application (at least according to the abstract) are only useful as intermediates or agrochemicals. There is no suggestion of the disclosed biological properties of the present compounds as inhibitors of p38-α kinase. These properties must be considered in evaluating patentability as set forth in *In re Papesch*, 315 F2d 381, 137 USPQ 43 (CCPA 1963).

Therefore, the combination of the Japanese application with the CRC Handbook is believed not to be germane in view of the structural and functional differences between the compounds claimed and those of the Japanese application set forth above.

Claim 1 was also rejected over the combination of WO 02/070491 in view of the CRC Handbook. The primary document is simply not citable. The present application is entitled at least to the benefit of its filing date which is 19 May 2000; the priority date, publication date and application date of WO 02/070491 are all later than the date to which the present application is entitled. There is no possible mechanism whereby the primary document could appropriately be cited, now or in the future, with respect to the present claims.

Double-Patenting

All claims were provisionally rejected as obviousness-type double-patenting over the pending claims of Serial No. 09/990,187 or certain claims of Serial No. 10/156,997 or Serial No. 09/989,991, all in view of U.S. 6,410,540, as well as 09/316,761 taken alone.

First, with respect to Serial Nos. 09/990,187 and 09/989,991, terminal disclaimers are enclosed.

Second, with respect to 10/156,997 which is a divisional of the present application, it is respectfully submitted that no terminal disclaimer is required as the claims in the '997 case are directed to compounds containing a piperidine moiety and those in the present application to compounds containing a piperazine moiety. In a restriction requirement mailed 4 May 2001, restriction was required between embodiments of group I wherein compounds contained a piperazine moiety and group II wherein the compounds contained a piperidine moiety. In view of this restriction requirement, it is believed that requiring a terminal disclaimer with respect to '997 is not proper.

With respect to 09/316,761 (now issued as U.S. patent 6,589,954) of which the present application is a continuation-in-part, reconsideration is respectfully requested. It will be noted that all of the compounds of the present invention specifically require the presence of a glyoxal-related moiety A, defined as W_iCOX_jY wherein Y is COR^2 or certain specified isosteres; most of the compounds indeed contain embodiments where i and j are 0 – *i.e.*, A is of the formula $COCOR^2$. While these compounds are very generically claimed in the '954 patent, the specific subspecies which contains a glyoxal substituent is not itself suggested. As this is a highly restricted species of the genus claimed in the '954 patent, it is not obvious over the much larger genus. It has been long-established that if a specific species contained in a genus is not suggested in the art, the species may be patentable thereover, even though the species may be a